Cycloalkyl derivatives as bone resorption inhibitors and vitronectin receptor antagonists

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Inventor(s): WEHNER VOLKMAR DR (DE); KNOLLE JOCHEN DR (DE); STILZ HANS ULRICH DR (DE); CARNIATO DENIS DR (FR); GOURVEST JEAN-FRANCOIS DR (FR); BODARY SARAH CARHERINE DR (US); GADEK THOMAS RICHARD DR (US); MCDOWELL ROBERT DR (US); PITTI ROBERT MAURICE (US)

Applicant(s): HOECHST AG (DE); GENENTECH INC (US)

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Abstract

Substituted cycloalkanes of formula R<1>YABDEF'C(R<4>)(R<5>)(CH2)qR<9> (I) and their salts are new. A = bond, 1-8C alkanediyl, NR<2>C(Q)NR<2>, NR<2>C(Q)Q, NR<2>S(O)nNR<2>, NR<2>S(O)nO, NR<2>S(O)n, 3-12C cycloalkanediyl, C IDENTICAL C, NR<2>CO, CONR<2>, 5-14C arylene-CONR<2>, O, S(O)n, 5-14C arylene, CO, 5-14C arylene-CO, NR<2>, SO2NR<2>, CO2, CR<2>=CR<3> or 5-14C arylene-S(O)n (all optionally mono- or disubstituted by 1-8C alkanediyl (sic), e.g. -1-8C alkanediyl-CONR<2>-1-8C alkanediyl, 1-8C alkanediyl-CONR<2> or CONR<2>-1-8C alkanediyl); Q = O or S; B = bond, 1-10C alkanediyl, CR<2>=CR<3> or C IDENTICAL C (all optionally mono- or disubstituted by 1-8C alkanediyl); D, F' = bond, 1-8C alkanediyl, or Q, NR<2>, CONR<2>, NR<2>CO, NR<2>C(Q)NR<2>, OCO, COO, CQ, S(O)n, S(O)2NR<2>, NR<2>S(O)n, CR<2>=CR<3>, C IDENTICAL C or CH(OH) (all optionally mono- or disubstituted by 1-8C alkanediyl); E = 6-membered aromatic group optionally containing 1-4 N atoms and optionally mono- to tetra-substituted by R<2>, R<3>, F, Cl, Br, I, NO2 and OH; Y = bond or NR<2>; R<1> = NR<2>C(=NR<2>)R<2>, C(=NR<2>)NR<2>R<3>, NR<2>C(=NR<2>)NR<2>R<3> or a 4-10 membered monocyclic or polycyclic aromatic or non-aromatic ring optionally containing 1-4 N, O and/or S atoms and optionally substituted by 1 or more R<11>, R<12>, R<13> and R<14>; R<2>, R<3> = H, 1-10C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkanediyl, 5-14C aryl, 5-14C aryl-1-8C alkanediyl, NH2, R<7>N(R<8>)OR<8>, R<7>OR<8>, R<7>COOR<8>, R<7>-5-14C arylene-R<8>, R<7>NR<8>R<8>, R<7>NR<8>-1-8C hydroxyalkyl, R<7>CONR<8>R<8>, R<7>NR<8>C(O)R<8>, R<7>COR<8>, C(=NR<8>)NR<8>R<8> or 1-18C alkylcarbonyloxy-1-6C alkanediyloxycarbonyl; R<4> = R<7>QR<6>, R<7>OCOR<6>, R<7>COOR<6>, R<7>-5-14C arylene-R<6>, R<7>NR<2>R<6>, R<7>NR<6>R<8>, R<7>OCONR<2>R<6>, R<7>NR<2>S(O)nR<6>, R<7>NR<2>COQR<6>, R<7>NR<2>C(O)R<6>, R<7>N(R<2>)C(O)N(R<2>)R<6>, R<7>N(R<2>)S(O)nN(R<2>)R<6>, R<7>S(O)nR<6>, R<7>C(O)R<6>, R<7>CONR<2>R<6>, R<7>S(O)nNR<2>R<6>, Cy or 1-8C alkyl substituted by Cy; Cy = monocyclic or polycyclic, saturated or mono- or poly-unsaturated 10-18C cycloalkyl optionally substituted by 1 or more Z'; Z' = 1-10C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkanediyl, 5-14C aryl, 5-14C aryl-1-8C alkanediyl, 1-8C alkoxy, 5-14C aryl-1-8C alkanediyloxy, 5-14C aryloxy, 1-8C alkylcarbonyloxy-1-4C alkanediyloxy, NH2, NH(1-8C alkyl), N(1-8C alkyl)2, 5-14C aryl-1-8C alkanediylamino, 5-14C arylamino, =Q, NO2, OH, F, Cl, Br or I; R<5> = H, F, 1-8C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkanediyl, 5-14C aryl or 5-14C aryl-1-8C alkanediyl; R<6> = Cy or 1-8C alkyl substituted by Cy; R<7> = bond or 1-8C alkanediyl; R<8> = H, 1-8C alkyl (optionally substituted by 1 or more F, or one 3-12C cycloalkyl or 5-14C aryl), 3-12C cycloalkyl or 5-14C aryl; R<9> = C(Q)R<10>, S(O)nR<10>, P(O)(R<10>)n or a 4-8 membered saturated or unsaturated heterocycle containing 1-4 N, O and/or S atoms; R<10> = OH, 1-8C

alkoxy(optionally substituted by 5-14C-aryl), 5-14C aryloxy, 1-8C alkylcarbonyloxy-1-4C alkanediyloxy, 5-14C aryl-1-8C alkanediylcarbonyloxy-1-6C alkanediyloxy, NH2, mono- or di- 1-8C alkylamino, 5-14C aryl-1-8C alkanediylamino, 1-8C dialkylaminocarbonylmethyleneoxy, 5-14C aryl-1-8C dialkylaminocarbonylmethyleneoxy, 5-14C arylamino or the residue of a L- or D-amino acid; R<11>-R<14> = H, 1-10C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkanediyl, 5-14C aryl, 5-14C aryl-1-8C alkanediyl, NH2, R<7>N(R<8>)OR<8>, R<7>OR<8>, R<7>COOR<8>, R<7>NR<8>R<8>, R<7>NR<2>-1-8C hydroxyalkyl, R<7>CONR<2>R<8>, R<7>COR<8>, NR<2>C(=NR<2>)NR<2>R<3>, C(=NR<2>)NR<2>R<3>, R<7>-5-14C arylene-R<8>, R<7>NR<2>COR<8> or Q; n = 1 or 2; q = 0 or 1.
